WO 2005/085253 PCT/JP2005/004266

46 CLAIMS

1. A pyrrolopyrimidine derivative represented by the following formula [I]:

$$\begin{array}{c}
X \\
N \\
N \\
R^2 \\
N \\
N \\
Ar
\end{array}$$
[I]

(wherein R^1 is C_{1-9} alkyl, C_{2-9} alkenyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl- C_{1-9} alkyl, di(C_{1-6} alkoxy)- C_{1-9} alkyl, hydroxy- C_{1-9} alkyl, cyano- C_{1-9} alkyl, carbamoyl- C_{1-9} alkyl, di(C_{1-6} alkyl)amino- C_{1-9} alkyl, aryl, heteroaryl, aryl- C_{1-9} alkyl or heteroaryl- C_{1-9} alkyl, in which said aryl and heteroaryl are optionally substituted with one to three substituents independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} alkylsulfonyl, aminosulfonyl, mono(C_{1-6} alkyl)aminosulfonyl, di(C_{1-6} alkyl)aminosulfonyl, halogen, C_{1-6} haloalkyl, cyano, nitro, -NR 1a R 1b , where R 1a and R 1b are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl and C_{1-6} alkylcarbonyl;

 R^2 is C_{1-6} alkyl or C_{1-6} haloalkyl;

 R^3 is hydrogen, $C_{1\text{-}6}$ alkyl, $C_{2\text{-}6}$ alkenyl, $C_{2\text{-}6}$ alkynyl, $C_{3\text{-}7}$ cycloalkyl, $C_{3\text{-}7}$ cycloalkyl, benzyl;

the bond between X and Y is a single bond or a double bond;

wherein (1) when the bond between X and Y is a single bond, X is CR^4R^5 or C=O; Y is CR^6R^7 , C=O, C=N-OR⁸ or C=CH-R⁹; (2) when the bond between X and Y is a double bond, X is CR^{10} ; Y is CR^{11} :

 R^4 and R^5 are the same or different, and independently are hydrogen or $C_{1\text{-}6}$ alkyl;

R⁶ and R⁷ are the same or different, and independently are hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, hydroxy, C₁₋₆alkylamino, di(C₁₋₆alkyl)amino-C₁₋₆alkyl, C₁₋₆alkylcarbonylamino, C₃₋₆cycloalkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, C₁₋₆alkylaminocarbonyl or C₁₋₆alkylaminocarbonylamino; or R⁶ and R⁷ are taken together to form C₃₋₆cycloalkyl, with the proviso that not both of CR⁴R⁵ and CR⁶R⁷

47

PCT/JP2005/004266

are CH₂;

 R^8 is hydrogen or C_{1-6} alkyl;

R⁹ is C₁₋₆alkyl, C₃₋₆cycloalkyl, aryl or heteroaryl, wherein said aryl and heteroaryl are optionally substituted with one to three substituents independently selected from the group consisting of halogen or C₁₋₆alkyl;

R¹⁰ is hydrogen or C₁₋₆alkyl;

R¹¹ is hydrogen, C₁₋₆alkyl or di(C₁₋₆alkyl)amino-C₁₋₆alkyl;

Ar is aryl or heteroaryl which aryl or heteroaryl is unsubstituted or substituted with 1 or more substituents, which are the same or different, selected from the group consisting of halogen, C₁₋₆alkyl, C₃₋₇cycloalkyl, C₂₋₆alkenyl, C₂₋₆alkenyl, C₁₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkylthio, C₁₋₆alkylsulfonyl, aminosulfonyl, mono(C₁₋₆alkyl)aminosulfonyl, di(C₁₋₆alkyl)aminosulfonyl, cyano, C₁₋₆haloalkyl, trifluoromethoxy, difluoromethoxy, fluoromethoxy and -N(R¹²)R¹³, wherein R¹² and R¹³ are the same or different, and independently are hydrogen or C₁₋₆alkyl), individual isomers thereof or racemic or non-racemic mixtures of isomers thereof, or pharmaceutically acceptable salts and hydrates thereof.

2. The pyrrolopyrimidine derivative according to claim 1 represented by the following formula [11]:

(wherein R^1 is C_{1-9} alkyl, C_{2-9} alkenyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl- C_{1-9} alkyl, di(C_{1-6} alkoxy)- C_{1-9} alkyl, hydroxy- C_{1-9} alkyl, cyano- C_{1-9} alkyl, carbamoyl- C_{1-9} alkyl, di(C_{1-6} alkyl)amino- C_{1-9} alkyl, aryl, heteroaryl, aryl- C_{1-9} alkyl or heteroaryl- C_{1-9} alkyl, in which said aryl and heteroaryl optionally substituted with one to three substituents independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} alkylsulfonyl, aminosulfonyl, mono(C_{1-6} alkyl)aminosulfonyl, di(C_{1-6} alkyl)aminosulfonyl, halogen, C_{1-6} haloalkyl, cyano, nitro, -NR 1a R 1b , where R^{1a} and R^{1b} are each independently selected from the group consisting of hydrogen, C_{1-6}

48

6alkyl and C₁₋₆alkylcarbonyl;

 R^2 is C_{1-6} alkyl or C_{1-6} haloalkyl;

 R^3 is hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl, benzyl;

R¹⁰ is hydrogen or C₁₋₆alkyl;

 R^{11} is hydrogen, $C_{1\text{-}6}$ alkyl or di($C_{1\text{-}6}$ alkyl)amino- $C_{1\text{-}6}$ alkyl;

Ar is aryl or heteroaryl which aryl or heteroaryl is unsubstituted or substituted with 1 or more substituents, which are the same or different, selected from the group consisting of halogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} alkylsulfonyl, aminosulfonyl, mono(C_{1-6} alkyl)aminosulfonyl, di(C_{1-6} alkyl)aminosulfonyl, cyano, halo C_{1-6} alkyl, trifluoromethoxy, difluoromethoxy, fluoromethoxy and $-N(R^{12})R^{13}$, wherein R^{12} and R^{13} are the same or different, and independently are hydrogen or C_{1-6} alkyl), individual isomers thereof or racemic or non-racemic mixtures of isomers thereof, or pharmaceutically acceptable salts and hydrates thereof.

- 3. The pyrrolopyrimidine derivative according to claim 2 represented by the formula [II], wherein R^1 is C_{1-9} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl- C_{1-6} alkyl, di(C_{3-7} cycloalkyl)- C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkyl, di(C_{1-6} alkoxy)- C_{1-6} alkyl, hydroxy- C_{1-6} alkyl, cyano- C_{1-6} alkyl, carbamoyl- C_{1-6} alkyl, di(C_{1-6} alkyl)amino- C_{1-6} alkyl, aryl- C_{1-6} alkyl or heteroaryl- C_{1-6} alkyl; R^2 is C_{1-6} alkyl; R^3 is hydrogen or C_{1-6} alkyl; R^{10} is hydrogen or C_{1-6} alkyl; R^{11} is hydrogen, C_{1-6} alkyl or di(C_{1-6} alkyl)amino- C_{1-6} alkyl; Ar is aryl or heteroaryl which aryl or heteroaryl is unsubstituted or substituted with one to three substituents, which are the same or different, selected from the group consisting of halogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} alkylthio, cyano, trifluoromethyl, trifluoromethoxy, difluoromethoxy, fluoromethoxy and -N(R^{12}) R^{13} , wherein R^{12} and R^{13} are the same or different, and independently are hydrogen or C_{1-6} alkyl, individual isomers thereof or racemic or non-racemic mixtures of isomers thereof, or pharmaceutically acceptable salts and hydrates thereof.
- 4. The pyrrolopyrimidine derivative according to claim 2 represented by the formula [II], wherein R¹ is C₁₋₉alkyl, C₃₋₇cycloalkyl, C₃₋₇cycloalkyl-C₁₋₆alkyl, di(C₃₋₇cycloalkyl)-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, di(C₁₋₆alkoxy)-C₁₋₆alkyl or aryl-C₁₋₆alkyl; R² is C₁₋₆alkyl; R³ is hydrogen or C₁₋₆alkyl; R¹⁰ is hydrogen or C₁₋₆alkyl; R¹¹

WO 2005/085253 PCT/JP2005/004266

49

is hydrogen or C_{1-6} alkyl; Ar is phenyl which phenyl is unsubstituted or substituted with one to three substituents, which are the same or different, selected from the group consisting of halogen, C_{1-3} alkyl, C_{1-3} alkoxy, C_{1-3} alkylthio, trifluoromethyl and $-N(R^{12})R^{13}$, wherein R^{12} and R^{13} are the same or different, and independently are hydrogen or C_{1-3} alkyl, individual isomers thereof or racemic or non-racemic mixtures of isomers thereof, or pharmaceutically acceptable salts and hydrates thereof.

- 5. The pyrrolopyrimidine derivative according to claim 2 represented by the formula [II], wherein R^1 is C_{1-9} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl- C_{1-6} alkyl, di(C_{3-7} cycloalkyl)- C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkyl, di(C_{1-6} alkoxy)- C_{1-6} alkyl or aryl- C_{1-6} alkyl; R^2 is C_{1-3} alkyl; R^3 is C_{1-3} alkyl; R^{10} is hydrogen; R^{11} is hydrogen; Ar is phenyl which phenyl is substituted with 2 or 3 substituents, which are the same or different, selected from the group consisting of halogen or C_{1-3} alkyl, individual isomers thereof or racemic or non-racemic mixtures of isomers thereof, or pharmaceutically acceptable salts and hydrates thereof.
- 6. An antagonist for CRF receptors, comprising a pyrrolopyrimidine derivative, a pharmaceutically acceptable salt thereof or its hydrate according to any one of claims 1 to 5, as an active ingredient.
- 7. Use of a pyrrolopyrimidine derivative, a pharmaceutically acceptable salt thereof or its hydrate according to any one of claim 1 to 5, for the manufacture of an antagonist for CRF receptors.